	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	4856	antibiotic same peptide	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/20 16:42			0
2	BRS	L2	370	definsin or protegrin or tachyplesin or polyphemusin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/20 16:45			0
3	BRS	L3	0	1 same beta$1stranded	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/20 16:43			0
4	BRS	L4	6	beta adj stranded	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/20 16:44			0
5	BRS	L5	28	1 same 2	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/20 16:44			0
6	BRS	L6	0	1 same 4	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/20 16:44			0
7	BRS	L7	2483	beta adj sheet	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/20 16:46			0
8	BRS	L8	11	1 same 7	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/20 16:55			0
9	BRS	L9	55	(2 or 8) same (disulfide or cysteine)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/20 17:07			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
10	BRS	L10	50378	active adj substance	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/20 17:09			0
11	BRS	L11	99930	(agent or compound) same (therapeutic or diagnostic)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/20 17:10			0
12	BRS	L12	0	9 same (10 or 11)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/20 17:10			0
13	BRS	L13	959079	vector$3 or transport$5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/20 17:11			0
14	BRS	L14	3	5 same 13	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/20 17:12			0

> d his

(FILE 'HOME' ENTERED AT 17:15:03 ON 20 SEP 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
17:15:26 ON 20 SEP 2002
L1 3889 S ANTIBIOTIC PEPTIDE
L2 1065 S DEFINSIN OR PROTEGRIN OR TACHYPLESIN OR POLYPHEMUSIN
L3 40880 S (BETA SHEET) OR (BETA STRAND)
L4 20 S L1 (P) L3
L5 266 S (L2 OR L4) (P) (DISULFIDE OR CYSTEINE)
L6 79 DUPLICATE REMOVE L5 (187 DUPLICATES REMOVED)
L7 16 S L5 (P) MODIF?
L8 34260 S (ACTIVE SUBSTANCE)
L9 52477 S (THERAPEUTIC AGENT) OR (DIAGNOSTIC AGENT)
L10 0 S (L8 OR L9) (P) L5 (P) (CONJUGATE OR COVALENT)
L11 1 S L5 (P) (VECTOR? OR TRANSPORT?)

=> log y

```
FILE 'HOME' ENTERED AT 17:15:03 ON 20 SEP 2002

=> file medline caplus biosis embase scisearch agricola
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                   0.21       0.21

FILE 'MEDLINE' ENTERED AT 17:15:26 ON 20 SEP 2002

FILE 'CAPLUS' ENTERED AT 17:15:26 ON 20 SEP 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE 'BIOSIS' ENTERED AT 17:15:26 ON 20 SEP 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'EMBASE' ENTERED AT 17:15:26 ON 20 SEP 2002
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FILE 'SCISEARCH' ENTERED AT 17:15:26 ON 20 SEP 2002
COPYRIGHT (C) 2002 Institute for Scientific Information (ISI) (R)

FILE 'AGRICOLA' ENTERED AT 17:15:26 ON 20 SEP 2002

=> s antibiotic peptide
L1         3889 ANTIBIOTIC PEPTIDE

=> s definsin or protegrin or tachyplesin or polyphemusin
L2         1065 DEFINSIN OR PROTEGRIN OR TACHYPLESIN OR POLYPHEMUSIN

=> s (beta sheet) or (beta strand)
L3        40880 (BETA SHEET) OR (BETA STRAND)

=> s l1 (p) l3
L4           20 L1 (P) L3

=> s (l2 or l4 ) (p) (disulfide or cysteine)
L5          266 (L2 OR L4 ) (P) (DISULFIDE OR CYSTEINE)

=> duplicate remove l5
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L5
L6            79 DUPLICATE REMOVE L5 (187 DUPLICATES REMOVED)

=> s l5 (p) modif?
L7           16 L5 (P) MODIF?

=> s (active substance)
L8        34260 (ACTIVE SUBSTANCE)

=> s (therapeutic agent) or (diagnostic agent)
L9        52477 (THERAPEUTIC AGENT) OR (DIAGNOSTIC AGENT)

=> s (l8 or l9) (p) l5 (p) (conjugate or covalent)
L10           0 (L8 OR L9) (P) L5 (P) (CONJUGATE OR COVALENT)

=> s l5 (p) (vector? or transport?)
L11           1 L5 (P) (VECTOR? OR TRANSPORT?)

=> d l11 1 ibib abs

L11  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         1996:200807  CAPLUS
DOCUMENT NUMBER:          124:282154
TITLE:                    Change in membrane permeability induced by protegrin
                          1: implication of disulfide bridges for pore formation
AUTHOR(S):                Mangoni, Matteo E.; Aumelas, Andre; Charnet, Pierre;
                          Roumestand, Christian; Chiche, Laurent; Despaux,
```

Ernest; Grassy, Gerard; Calas, Bernard; Chavanieu, Alain

CORPORATE SOURCE: Centre de Recherches de Biochimie Macromoleculaire, CNRS-INSERM, UPR 9008, U249, BP 5051 route de Mende, Montpellier, 34033, Fr.

SOURCE: FEBS Letters (1996), 383(1,2), 93-8
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Protegrin 1 (PG-1) is a naturally occurring cationic antimicrobial peptide that is 18 residues long, has an aminated carboxy terminus and contains two disulfide bridges. Here, the authors investigated the antimicrobial activity of PG-1 and three linear analogs. Then, the membrane permeabilization induced by these peptides was studied upon Xenopus laevis oocytes by electrophysiol. methods. From the results obtained, the authors concluded that protegrin is able to form anion channels. Moreover, it seems clear that the presence of disulfide bridges is a prerequisite for the pore formation at the membrane level and not for the antimicrobial activity.

=> d his

(FILE 'HOME' ENTERED AT 17:15:03 ON 20 SEP 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 17:15:26 ON 20 SEP 2002

```
L1          3889 S ANTIBIOTIC PEPTIDE
L2          1065 S DEFINSIN OR PROTEGRIN OR TACHYPLESIN OR POLYPHEMUSIN
L3         40880 S (BETA SHEET) OR (BETA STRAND)
L4            20 S L1 (P) L3
L5           266 S (L2 OR L4 ) (P) (DISULFIDE OR CYSTEINE)
L6            79 DUPLICATE REMOVE L5 (187 DUPLICATES REMOVED)
L7            16 S L5 (P) MODIF?
L8         34260 S (ACTIVE SUBSTANCE)
L9         52477 S (THERAPEUTIC AGENT) OR (DIAGNOSTIC AGENT)
L10            0 S (L8 OR L9) (P) L5 (P) (CONJUGATE OR COVALENT)
L11            1 S L5 (P) (VECTOR? OR TRANSPORT?)
```

=> d l7 1-16 ibib abs

L7 ANSWER 1 OF 16 MEDLINE

ACCESSION NUMBER: 2002061833 MEDLINE
DOCUMENT NUMBER: 21633976 PubMed ID: 11771999

TITLE: Overexpression and structural study of the cathelicidin motif of the protegrin-3 precursor.

AUTHOR: Sanchez Jean Frederic; Wojcik Franck; Yang Yin-Shan; Strub Marie-Paule; Strub Jean Marc; Van Dorsselaer Alain; Martin Marianne; Lehrer Robert; Ganz Tomas; Chavanieu Alain; Calas Bernard; Aumelas Andre

CORPORATE SOURCE: Centre de Biochimie Structurale, UMR 5048 CNRS-UM1/UMR 554 INSERM-UM1, Universite Montpellier 1, Faculte de Pharmacie, 15 avenue Charles Flahault, 34093 Montpellier Cedex 5, France.

SOURCE: BIOCHEMISTRY, (2002 Jan 8) 41 (1) 21-30.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020130
Entered Medline: 20020129

AB Numerous precursors of antibacterial peptides with unrelated sequences share a similar prosequence of 96-101 residues, referred to as the cathelicidin motif. The structure of this widespread motif has not yet been reported. The cathelicidin motif of ***protegrin*** -3 (ProS) was overexpressed in Escherichia coli as a His-tagged protein to facilitate its purification. The His tag was then removed by thrombin cleavage. In addition, the complete proprotegrin-3 (ProS-PG-3) (120 residues) was

overexpressed in baculovirus-infected insect cells. As it contained the antibacterial peptide ***protegrin*** -3 in its C-terminal part, ProS-PG-3 contained four ***disulfide*** bonds. At neutral pH, ProS and ProS-PG-3 adopted two slowly exchanging conformations that existed in a ratio of 55/45. This ratio was progressively ***modified*** at acidic pH to reach a 90/10 value at pH 3.0, suggesting that electrostatic interactions are involved in such a conformational change. Therefore, the structural study of the main conformer was undertaken at pH 3.0 by circular dichroism, mass spectrometry, and homo- and heteronuclear NMR. In parallel, a model for the ProS structure was built from the X-ray structure of the chicken cystatin. ProS and the chicken cystatin share two conserved ***disulfide*** bonds as well as a high conservation of hydrophobic residues. The ProS model features the conservation of a hydrophobic core made of the interface between the N-terminal helix and the wrapping beta-sheet. Although the full assignment of the main conformer of ProS could not be obtained, available NMR data validated the presence of the N-terminal helix and of a four-stranded beta-sheet, in agreement with the cystatin fold. Moreover, we clearly demonstrated that ProS and ProS-PG-3 share the same global structure, suggesting that the presence of the highly constrained beta-hairpin of ***protegrin*** does not significantly ***modify*** the structure of the cathelicidin motif of the ***protegrin*** precursor.

L7 ANSWER 2 OF 16 MEDLINE
ACCESSION NUMBER: 1998261485 MEDLINE
DOCUMENT NUMBER: 98261485 PubMed ID: 9596706
TITLE: Activity of protegrins against yeast-phase Candida albicans.
AUTHOR: Cho Y; Turner J S; Dinh N N; Lehrer R I
CORPORATE SOURCE: Department of Medicine, UCLA School of Medicine, Los Angeles, California 90095-1690, USA.
CONTRACT NUMBER: AI 22839 (NIAID)
AI 37945 (NIAID)
SOURCE: INFECTION AND IMMUNITY, (1998 Jun) 66 (6) 2486-93.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980708
Last Updated on STN: 19980708
Entered Medline: 19980625

AB We used a two-stage radial diffusion assay to perform a structure-activity study of the antifungal effects of ***protegrin*** -1 (PG-1) on yeast-phase Candida albicans. While doing so, we computed MICs from the radial diffusion assay data by three methods and compared the respective values with results from colony count and broth microdilution assays. This allowed us to identify several technical ***modifications*** that improved the sensitivity and accuracy of radial diffusion assays. We found that both PG-1 and enantiomeric PG-1 (composed exclusively of D-amino acids) were potently fungicidal for yeast-phase C. albicans. The ***protegrins*** PG-2, -3, and -5, but not PG-4, were as effective as PG-1. At least one intramolecular ***disulfide*** bond was required to retain optimal candidacidal activity at physiological NaCl concentrations. Truncated variants of PG-1 that lacked its first four residues showed decreased candidacidal activity, although their activity against bacteria was substantially intact. Altering the beta-turn region (residues 9 to 12) of PG-1 or its variants further decreased candidacidal activity. These studies suggest that only 12 residues are needed to endow ***protegrin*** molecules with strong antibacterial activity and that at least 4 additional residues are needed to add potent antifungal properties. Thus, the 16-residue ***protegrin*** PG-2 likely represents the minimal structure needed for broad-spectrum antimicrobial activity encompassing bacteria and fungi.

L7 ANSWER 3 OF 16 MEDLINE
ACCESSION NUMBER: 1998259478 MEDLINE
DOCUMENT NUMBER: 98259478 PubMed ID: 9597190
TITLE: Downsizing of an HIV-cell fusion inhibitor, T22 ([Tyr5,12, Lys7]-polyphemusin II), with the maintenance of anti-HIV activity and solution structure.

AUTHOR: Tamamura H; Wak[redacted]M; Imai M; Otaka A; Ibuka T; Wa[redacted]K; Miyamoto K; Mat[redacted]moto A; Murakami T; Nakashima H[redacted]amamoto N; Fujii N

CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Japan. tamamura@pharm.kyoto-u.ac.jp or. nfujii@pharm.kyoto-u.ac.jp

SOURCE: BIOORGANIC AND MEDICINAL CHEMISTRY, (1998 Apr) 6 (4) 473-9. Journal code: 9413298. ISSN: 0968-0896.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; AIDS

ENTRY MONTH: 199807

ENTRY DATE: Entered STN: 19980731
Last Updated on STN: 19980731
Entered Medline: 19980723

AB T22 ([Tyr5,12,Lys7]- ***polyphemusin*** II) has been shown to have strong anti-human immunodeficiency virus (HIV) activity comparable to that of 3'-azido-2',3'-dideoxythymidine (AZT). T22, an 18-residue peptide amide, takes an antiparallel beta-sheet structure that is maintained by two ***disulfide*** bridges. Herein we synthesized several shortened analogs of T22 in order to search for a more suitable lead compound. A 14-residue analog having one ***disulfide*** bridge, TW70 (des-[Cys8,13, Tyr9,12]-[D-Lys10, Pro11]-T22), was found to have highly potent activity comparable to that of T22, and to take an antiparallel beta-sheet structure similar to that of T22. This indicates that the molecular size of T22 can be reduced without loss of activity or significant change in the secondary structure, and that TW70 may represent a novel lead compound. Furthermore, ***modifying*** the N-terminal alpha-amino group of TW70 with a fluoresceinthiocarbamoyl group, and the epsilon-amino group of D-Lys8 at the turn portion with a 5-aminopentanoyl group remarkably increased the selectivity index (50% cytotoxic concentration/50% effective concentration).

L7 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:881148 CAPLUS

DOCUMENT NUMBER: 136:146754

TITLE: Overexpression and Structural Study of the Cathelicidin Motif of the Protegrin-3 Precursor

AUTHOR(S): Sanchez, Jean Frederic; Wojcik, Franck; Yang, Yin-Shan; Strub, Marie-Paule; Strub, Jean Marc; Van Orsselaer, Alain; Martin, Marianne; Lehrer, Robert; Ganz, Tomas; Chavanieu, Alain; Calas, Bernard; Aumelas, Andre

CORPORATE SOURCE: Centre de Biochimie Structurale, UMR 5048 CNRS-UM1/UMR 554 INSERM-UM1, Universite Montpellier 1, Montpellier, 34093, Fr.

SOURCE: Biochemistry (2002), 41(1), 21-30
CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Numerous precursors of antibacterial peptides with unrelated sequences share a similar prosequence of 96-101 residues, referred to as the cathelicidin motif. The structure of this widespread motif has not yet been reported. The cathelicidin motif of ***protegrin*** -3 (ProS) was overexpressed in Escherichia coli as a His-tagged protein to facilitate its purifn. The His tag was then removed by thrombin cleavage. In addn., the complete proprotegrin-3 (ProS-PG-3) (120 residues) was overexpressed in baculovirus-infected insect cells. As it contained the antibacterial peptide ***protegrin*** -3 in its C-terminal part, ProS-PG-3 contained four ***disulfide*** bonds. At neutral pH, ProS and ProS-PG-3 adopted two slowly exchanging conformations that existed in a ratio of 55/45. This ratio was progressively ***modified*** at acidic pH to reach a 90/10 value at pH 3.0, suggesting that electrostatic interactions are involved in such a conformational change. Therefore, the structural study of the main conformer was undertaken at pH 3.0 by CD, mass spectrometry, and homo- and heteronuclear NMR. In parallel, a model for the ProS structure was built from the x-ray structure of the chicken cystatin. ProS and the chicken cystatin share two conserved ***disulfide*** bonds as well as a high conservation of hydrophobic residues. The ProS model features the conservation of a hydrophobic core made of the

interface between the N-terminal helix and the wrapping .beta.-sheet. Although the full assignment of the main conformer of ProS could not be obtained, available NMR data validated the presence of the N-terminal helix and of a four-stranded .beta.-sheet, in agreement with the cystatin fold. Moreover, we clearly demonstrated that ProS and ProS-PG-3 share the same global structure, suggesting that the presence of the highly constrained .beta.-hairpin of ***protegrin*** does not significantly ***modify*** the structure of the cathelicidin motif of the ***protegrin*** precursor.
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:363142 CAPLUS
DOCUMENT NUMBER: 129:107961
TITLE: Activity of protegrins against yeast-phase Candida albicans
AUTHOR(S): Cho, Yoon; Turner, Jeffrey S.; Dinh, Nhu-Nguyen; Lehrer, Robert I.
CORPORATE SOURCE: Department of Medicine, UCLA School of Medicine, Los Angeles, CA, 90095-1690, USA
SOURCE: Infection and Immunity (1998), 66(6), 2486-2493
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors used a two-stage radial diffusion assay to perform a structure-activity study of the antifungal effects of ***protegrin*** -1 (PG-1) on yeast-phase Candida albicans. While doing so, the authors computed MICs from the radial diffusion assay data by three methods and compared the resp. values with results from colony count and broth microdilution assays. This allowed the authors to identify several tech. ***modifications*** that improved the sensitivity and accuracy of radial diffusion assays. The authors found that both PG-1 and enantiomeric PG-1 (composed exclusively of D-amino acids) were potently fungicidal for yeast-phase C. albicans. The ***protegrins*** PG-2, -3, and -5, but not PG-4, were as effective as PG-1. At least one intramol. ***disulfide*** bond was required to retain optimal candidacidal activity at physiol. NaCl concns. Truncated variants of PG-1 that lacked its first four residues showed decreased candidacidal activity, although their activity against bacteria was substantially intact. Altering the .beta.-turn region (residues 9 to 12) of PG-1 or its variants further decreased candidacidal activity. These studies suggest that only 12 residues are needed to endow ***protegrin*** mols. with strong antibacterial activity and that at least 4 addnl. residues are needed to add potent antifungal properties. Thus, the 16-residue ***protegrin*** PG-2 likely represents the minimal structure needed for broad-spectrum antimicrobial activity encompassing bacteria and fungi.

L7 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:274555 CAPLUS
DOCUMENT NUMBER: 129:28201
TITLE: Downsizing of an HIV-cell fusion inhibitor, T22 ([Tyr5,12, Lys7]-polyphemusin II), with the maintenance of anti-HIV activity and solution structure
AUTHOR(S): Tamamura, Hirokazu; Waki, Michinori; Imai, Makoto; Otaka, Akira; Ibuka, Toshiro; Waki, Koji; Miyamoto, Kenji; Matsumoto, Akiyoshi; Murakami, Tsutomu; Nakashima, Hideki; Yamamoto, Naoki; Fujii, Nobutaka
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-01, Japan
SOURCE: Bioorganic & Medicinal Chemistry (1998), 6(4), 473-479
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB T22, [Tyr5,12, Lys7]- ***polyphemusin*** II, has been shown to have strong anti-human immunodeficiency virus (HIV) activity comparable to that of AZT, 3'-azido-2',3'-dideoxythymidine. T22, an 18-residue peptide amide, takes an antiparallel .beta.-sheet structure that is maintained by two ***disulfide*** bridges. The authors have synthesized several

shortened analogs of T22 in order to search for a more suitable lead compd. A 14-residue peptide analog having one ***disulfide*** bridge, TW70 (des-[Cys8,13,Tyr9,12]-[D-Lys10, Pro11]-T22) was found to have highly potent activity comparable to that of T22, and to take an antiparallel .beta.-sheet structure similar to that of T22. Thus, the mol. size of T22 can be reduced without loss of activity or significant change in the secondary structure, and that TW70 may represent a novel lead compd. Furthermore, ***modifying*** the N-terminal .alpha.-amino group of TW70 with a fluoresceinthiocarbamoyl group, and the .epsilon.-amino group of D-Lys8 at the turn portion with a 5-aminopentanoyl group remarkably increased the selectivity index (50% cytotoxic concn./50% effective concn.).

L7 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:55470 CAPLUS
DOCUMENT NUMBER: 128:127091
TITLE: Immunoglobulins reactive with protegrins
INVENTOR(S): Lehrer, Robert I.; Harwig, Sylvia S. L.
PATENT ASSIGNEE(S): University of California, USA
SOURCE: U.S., 37 pp., Cont.-in-part of U.S. Ser. No. 182,483.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5708145	A	19980113	US 1994-243879	19940517
US 5464823	A	19951107	US 1993-95769	19930726
US 5693486	A	19971202	US 1994-182483	19940113
WO 9503325	A1	19950202	WO 1994-US8305	19940720
W: AU, BB, BG, BR, BY, CA, CH, CN, CZ, FI, HU, JP, KP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9474033	A1	19950220	AU 1994-74033	19940720
AU 689487	B2	19980402		
EP 711305	A1	19960515	EP 1995-906203	19940720
EP 711305	B1	20011121		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09503383	T2	19970408	JP 1994-505343	19940720
AT 209215	E	20011215	AT 1995-906203	19940720
US 5804558	A	19980908	US 1995-499523	19950707
US 5994306	A	19991130	US 1996-752852	19961121

PRIORITY APPLN. INFO.:
US 1993-93926 B2 19930720
US 1993-95769 A2 19930726
US 1994-182483 A2 19940113
US 1994-243879 A 19940517
WO 1994-US8305 W 19940720
US 1995-451832 B2 19950526
US 1995-499523 A2 19950707
US 1995-562346 B2 19951122
US 1996-649811 B2 19960517
US 1996-690921 B2 19960801

AB Peptide-based compds. contg. four invariant ***cysteine*** residues which have been optionally oxidized to contain two intramol. ***disulfide*** bonds, or ***modified*** forms where the ***cysteines*** are replaced are useful as preservatives and in preventing, treating, or ameliorating viral or microbial infection in animals and plants, and in inactivating endotoxin. Antibodies for the ***protegrins*** are also claimed. Three ***protegrin*** peptides PG-1, PG-2 and PG-3 were purified, characterized, and tested for their antimicrobial activity, ability to bind endotoxin, and eye treatment (in contact lens soln.). Also described was mol. cloning of cDNA clones encoding PG-1, PG-2, PG-3, and PG-4.

L7 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:508054 CAPLUS
DOCUMENT NUMBER: 122:230760
TITLE: Protegrins and their preparation and uses
INVENTOR(S): Lehrer, Robert L.; Harwig, Sylvia S. L.; Kokryakov,

Vladimir N[redacted]
PATENT ASSIGNEE(S): University of California, USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9503325	A1	19950202	WO 1994-US8305	19940720
W: AU, BB, BG, BR, BY, CA, CH, CN, CZ, FI, HU, JP, KP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5464823	A	19951107	US 1993-95769	19930726
US 5693486	A	19971202	US 1994-182483	19940113
US 5708145	A	19980113	US 1994-243879	19940517
AU 9474033	A1	19950220	AU 1994-74033	19940720
AU 689487	B2	19980402		
EP 711305	A1	19960515	EP 1995-906203	19940720
EP 711305	B1	20011121		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09503383	T2	19970408	JP 1994-505343	19940720
AT 209215	E	20011215	AT 1995-906203	19940720
US 5994306	A	19991130	US 1996-752852	19961121

PRIORITY APPLN. INFO.:

US 1993-93926	A	19930720
US 1993-95769	A	19930726
US 1994-182483	A	19940113
US 1994-243879	A	19940517
WO 1994-US8305	W	19940720
US 1995-451832	B2	19950526
US 1995-499523	A2	19950707
US 1995-562346	B2	19951122
US 1996-649811	B2	19960517
US 1996-690921	B2	19960801

AB Peptide-based compds. contg. four invariant ***cysteine*** residues which have been optionally oxidized to contain two intramol. ***disulfide*** bonds, or ***modified*** forms where the ***cysteines*** are replaced, are useful as preservatives and in preventing, treating, or ameliorating viral or microbial infection in animals and plants, and in inactivating endotoxin. Exemplary peptides include the following in purified and isolated forms: RGGRLCYCRRRFCVCVGR, RGGRLCYCRRFCICV, RGGGLCYCRRRFCVCVGR, and RGGRLCYCRGWICFCVGR. Isolation of the cDNA encoding ***protegrins*** from pig leukocytes is also shown.

L7 ANSWER 9 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:138101 BIOSIS
DOCUMENT NUMBER: PREV200200138101
TITLE: Overexpression and structural study of the cathelicidin motif of the protegrin-3 precursor.
AUTHOR(S): Sanchez, Jean Frederic; Wojcik, Franck; Yang, Yin-Shan; Strub, Marie-Paule; Strub, Jean Marc; Van Dorsselaer, Alain; Martin, Marianne; Lehrer, Robert; Ganz, Tomas; Chavanieu, Alain; Calas, Bernard; Aumelas, Andre (1)
CORPORATE SOURCE: (1) Centre de Biochimie Structurale, UMR 5048 CNRS-UM1/UMR 554 INSERM-UM1, Faculte de Pharmacie, Universite Montpellier 1, 15 avenue Charles Flahault, 34093, Montpellier Cedex, 5: aumelas@cbs.univ-montp1.fr France
SOURCE: Biochemistry, (January 8, 2002) Vol. 41, No. 1, pp. 21-30. http://pubs.acs.org/journals/bichaw/. print.
ISSN: 0006-2960.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Numerous precursors of antibacterial peptides with unrelated sequences share a similar prosequence of 96-101 residues, referred to as the cathelicidin motif. The structure of this widespread motif has not yet been reported. The cathelicidin motif of ***protegrin*** -3 (ProS) was overexpressed in Escherichia coli as a His-tagged protein to facilitate its purification. The His tag was then removed by thrombin cleavage. In addition, the complete proprotegrin-3 (ProS-PG-3) (120 residues) was

overexpressed in baculovirus-infected insect cells. As it contained the antibacterial peptide ***protegrin*** -3 in its C-terminal part, ProS-PG-3 contained four ***disulfide*** bonds. At neutral pH, ProS and ProS-PG-3 adopted two slowly exchanging conformations that existed in a ratio of 55/45. This ratio was progressively ***modified*** at acidic pH to reach a 90/10 value at pH 3.0, suggesting that electrostatic interactions are involved in such a conformational change. Therefore, the structural study of the main conformer was undertaken at pH 3.0 by circular dichroism, mass spectrometry, and homo- and heteronuclear NMR. In parallel, a model for the ProS structure was built from the X-ray structure of the chicken cystatin. ProS and the chicken cystatin share two conserved ***disulfide*** bonds as well as a high conservation of hydrophobic residues. The ProS model features the conservation of a hydrophobic core made of the interface between the N-terminal helix and the wrapping beta-sheet. Although the full assignment of the main conformer of ProS could not be obtained, available NMR data validated the presence of the N-terminal helix and of a four-stranded beta-sheet, in agreement with the cystatin fold. Moreover, we clearly demonstrated that ProS and ProS-PG-3 share the same global structure, suggesting that the presence of the highly constrained beta-hairpin of ***protegrin*** does not significantly ***modify*** the structure of the cathelicidin motif of the ***protegrin*** precursor.

L7 ANSWER 10 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:304892 BIOSIS
DOCUMENT NUMBER: PREV199800304892
TITLE: Activity of protegrins against yeast-phase Candida albicans.
AUTHOR(S): Cho, Yoon; Turner, Jeffrey S.; Dinh, Nhu-Nguyen; Lehrer, Robert I. (1)
CORPORATE SOURCE: (1) Dep. Med., Box 951690, 10833 LeConte Ave, Los Angeles, CA 90095-1690 USA
SOURCE: Infection and Immunity, (June, 1998) Vol. 66, No. 6, pp. 2486-2493.
ISSN: 0019-9567.
DOCUMENT TYPE: Article
LANGUAGE: English
AB We used a two-stage radial diffusion assay to perform a structure-activity study of the antifungal effects of ***protegrin*** -1 (PG-1) on yeast-phase Candida albicans. While doing so, we computed MICs from the radial diffusion assay data by three methods and compared the respective values with results from colony count and broth microdilution assays. This allowed us to identify several technical ***modifications*** that improved the sensitivity and accuracy of radial diffusion assays. We found that both PG-1 and enantiomeric PG-1 (composed exclusively of D-amino acids) were potently fungicidal for yeast-phase C. albicans. The ***protegrins*** PG-2, -3, and -5, but not PG-4, were as effective as PG-1. At least one intramolecular ***disulfide*** bond was required to retain optimal candidacidal activity at physiological NaCl concentrations. Truncated variants of PG-1 that lacked its first four residues showed decreased candidacidal activity, although their activity against bacteria was substantially intact. Altering the beta-turn region (residues 9 to 12) of PG-1 or its variants further decreased candidacidal activity. These studies suggest that only 12 residues are needed to endow ***protegrin*** molecules with strong antibacterial activity and that at least 4 additional residues are needed to add potent antifungal properties. Thus, the 16-residue ***protegrin*** PG-2 likely represents the minimal structure needed for broad-spectrum antimicrobial activity encompassing bacteria and fungi.

L7 ANSWER 11 OF 16 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002021664 EMBASE
TITLE: Overexpression and structural study of the cathelicidin motif of the protegrin-3 precursor.
AUTHOR: Sanchez J.F.; Wojcik F.; Yang Y.-S.; Strub M.-P.; Strub J.M.; Van Dorsselaer A.; Martin M.; Lehrer R.; Ganz T.; Chavanieu A.; Calas B.; Aumelas A.
CORPORATE SOURCE: A. Aumelas, Centre de Biochimie Structurale, UMR 5048 CNRS-UM1/UMR 554 INSERM-UM1, Universite Montpellier 1, 15 avenue Charles Flahault, 34093 Montpellier Cedex 5, France. aumelas@cbs:univ-montp1.fr
SOURCE: Biochemistry, (8 Jan 2002) 41/1 (21-30).

Refs: 52
ISSN: 0006-2960 CODEN: BICHAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Numerous precursors of antibacterial peptides with unrelated sequences share a similar prosequence of 96-101 residues, referred to as the cathelicidin motif. The structure of this widespread motif has not yet been reported. The cathelicidin motif of ***protegrin*** -3 (ProS) was overexpressed in Escherichia coli as a His-tagged protein to facilitate its purification. The His tag was then removed by thrombin cleavage. In addition, the complete proprotegrin-3 (ProS-PG-3) (120 residues) was overexpressed in baculovirus-infected insect cells. As it contained the antibacterial peptide ***protegrin*** -3 in its C-terminal part, ProS-PG-3 contained four ***disulfide*** bonds. At neutral pH, ProS and ProS-PG-3 adopted two slowly exchanging conformations that existed in a ratio of 55/45. This ratio was progressively ***modified*** at acidic pH to reach a 90/10 value at pH 3.0, suggesting that electrostatic interactions are involved in such a conformational change. Therefore, the structural study of the main conformer was undertaken at pH 3.0 by circular dichroism, mass spectrometry, and homo- and heteronuclear NMR. In parallel, a model for the ProS structure was built from the X-ray structure of the chicken cystatin. ProS and the chicken cystatin share two conserved ***disulfide*** bonds as well as a high conservation of hydrophobic residues. The ProS model features the conservation of a hydrophobic core made of the interface between the N-terminal helix and the wrapping .beta.-sheet. Although the full assignment of the main conformer of ProS could not be obtained, available NMR data validated the presence of the N-terminal helix and of a four-stranded .beta.-sheet, in agreement with the cystatin fold. Moreover, we clearly demonstrated that ProS and ProS-PG-3 share the same global structure, suggesting that the presence of the highly constrained .beta.-hairpin of ***protegrin*** does not significantly ***modify*** the structure of the cathelicidin motif of the ***protegrin*** precursor.

L7 ANSWER 12 OF 16 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998189112 EMBASE
TITLE: Activity of protegrins against yeast-phase Candida albicans.
AUTHOR: Cho Y.; Turner J.S.; Dinh N.-N.; Lehrer R.I.
CORPORATE SOURCE: R.I. Lehrer, Department of Medicine, Box 951690, 10833 LeConte Ave., Los Angeles, CA 90095-1690, United States. rlehrer@medl.medsch.ucla.edu
SOURCE: Infection and Immunity, (1998) 66/6 (2486-2493).
Refs: 38
ISSN: 0019-9567 CODEN: INFIBR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB We used a two-stage radial diffusion assay to perform a structure-activity study of the antifungal effects of ***protegrin*** -1 (PG-1) on yeast- phase Candida albicans. While doing so, we computed MICs from the radial diffusion assay data by three methods and compared the respective values with results from colony count and broth microdilution assays. This allowed us to identify several technical ***modifications*** that improved the sensitivity and accuracy of radial diffusion assays. We found that both PG-1 and enantiomeric PG-1 (composed exclusively of D-amino acids) were potently fungicidal for yeast-phase C. albicans. The ***protegrins*** PG-2, -3, and -5, but not PG-4, were as effective as PG-1. At least one intramolecular ***disulfide*** bond was required to retain optimal candidacidal activity at physiological NaCl concentrations. Truncated variants of PG-1 that lacked its first four residues showed decreased candidacidal activity, although their activity against bacteria was substantially intact. Altering the .beta.-turn region (residues 9 to 12) of PG-1 or its variants further decreased candidacidal activity. These studies suggest that only 12 residues are needed to endow

protegrin molecules with strong antibacterial activity and that at least 4 additional residues are needed to add potent antifungal properties. Thus, the 16-residue ***protegrin*** PG-2 likely represents the minimal structure needed for broad-spectrum antimicrobial activity encompassing bacteria and fungi.

L7 ANSWER 13 OF 16 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998131029 EMBASE
TITLE: Downsizing of an HIV-cell fusion inhibitor, T22 ([tyr5'12, lys7]- polyphemusin II), with the maintenance of anti-HIV activity and solution structure.
AUTHOR: Tamamura H.; Waki M.; Imai M.; Otaka A.; Ibuka T.; Waki K.; Miyamoto K.; Matsumoto A.; Murakami T.; Nakashima H.; Yamamoto N.; Fujii N.
CORPORATE SOURCE: H. Tamamura, Graduate Sch. of Pharmaceut. Sci., Kyoto University, Sakyo-ku, Kyoto 606-01, Japan. tamamura@pharm.kyoto-u.ac.jp
SOURCE: Bioorganic and Medicinal Chemistry, (1998) 6/4 (473-479). Refs: 22
ISSN: 0968-0896 CODEN: BMECEP
PUBLISHER IDENT.: S 0968-0896(97)10055-4
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB T22 ([Tyr5,12, Lys7]- ***polyphemusin*** II) has been shown to have strong anti-human immunodeficiency virus (HIV) activity comparable to that of 3'- azido-2',3'-dideoxythymidine (AZT). T22, an 18-residue peptide amide, takes an antiparallel .beta.-sheet structure that is maintained by two ***disulfide*** bridges. Herein we synthesized several shortened analogs of T22 in order to search for a more suitable lead compound. A 14-residue analog having one ***disulfide*** bridge, TW70 (des-[Cys8,13, Tyr9,12]-[D-Lys10, Pro11]- T22), was found to have highly potent activity comparable to that of T22, and to take an antiparallel .beta.-sheet structure similar to that of T22. This indicates that the molecular size of T22 can be reduced without loss of activity or significant change in the secondary structure, and that TW70 may represent a novel lead compound. Furthermore, ***modifying*** the N-terminal .alpha.- amino group of TW70 with a fluoresceinthiocarbamoyl group, and the .epsilon.-amino group of D-Lys8 at the turn portion with a 5-aminopentanoyl group remarkably increased the selectivity index (50% cytotoxic concentration/50% effective concentration).

L7 ANSWER 14 OF 16 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2002:65237 SCISEARCH
THE GENUINE ARTICLE: 510PM
TITLE: Overexpression and structural study of the cathelicidin motif of the protegrin-3 precursor
AUTHOR: Sanchez J F; Wojcik F; Yang Y S; Strub M P; Strub J M; Van Dorsselaer A; Martin M; Lehrer R; Ganz T; Chavanieu A; Calas B; Aumelas A (Reprint)
CORPORATE SOURCE: Univ Montpellier 1, INSERM UM1, Fac Pharm, UMR 554, Ctr Biochim Struct, CNRS UM1, UMR 5048, 15 Ave Charles Flahault, F-34093 Montpellier 5, France (Reprint); Univ Montpellier 1, INSERM UM1, Fac Pharm, UMR 554, Ctr Biochim Struct, CNRS UM1, UMR 5048, F-34093 Montpellier 5, France; ECPM, Lab Spectrometrie Mass Bioorgan, F-67087 Strasbourg, France; Univ Montpellier 2, CNRS, UMR 5539, F-34095 Montpellier 05, France; Hlth Sci Ctr, Dept Med, Los Angeles, CA 90095 USA
COUNTRY OF AUTHOR: France; USA
SOURCE: BIOCHEMISTRY, (8 JAN 2002) Vol. 41, No. 1, pp. 21-30. Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA.
ISSN: 0006-2960.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 51
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Numerous precursors of antibacterial peptides with unrelated sequences

share a similar prosequence of [redacted]6-101 residues, referred to as [redacted]e cathelicidin motif. The struct[redacted]e of this widespread motif has not yet been reported. The cathelicidin motif of ***protegrin*** -3 (ProS) was overexpressed in Escherichia coli as a His-tagged protein to facilitate its purification. The His tag was then removed by thrombin cleavage. In addition, the complete proprotegrin-3 (ProS-PG-3) (120 residues) was overexpressed in baculovirus-infected insect cells. As it contained the antibacterial peptide ***protegrin*** -3 in its C-terminal part, ProS-PG-3 contained four ***disulfide*** bonds. At neutral PH, ProS and ProS-PG-3 adopted two slowly exchanging conformations that existed in a ratio of 55/45. This ratio was progressively ***modified*** at acidic PH to reach a 90/10 value at PH 3.0, suggesting that electrostatic interactions are involved in such a conformational change. Therefore, the structural study of the main conformer was undertaken at PH 3.0 by circular dichroism, mass spectrometry, and homo- and heteronuclear NMR. In parallel., a model for the ProS structure was built from the X-ray structure of the chicken cystatin. ProS and the chicken cystatin share two conserved ***disulfide*** bonds as well as a high conservation of hydrophobic residues. The ProS model features the conservation of a hydrophobic core made of the interface between the N-terminal helix and the wrapping beta-sheet. Although the full assignment of the main conformer of ProS could not be obtained, available NMR data validated the presence of the N-terminal helix and of a four-stranded beta-sheet, in agreement with the cystatin fold. Moreover, we clearly demonstrated that ProS and ProS-PG-3 share the same global structure, suggesting that the presence of the highly constrained beta-hairpin of ***protegrin*** does not significantly ***modify*** the structure of the cathelicidin motif of the ***protegrin*** precursor.

L7 ANSWER 15 OF 16 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 1998:414710 SCISEARCH
THE GENUINE ARTICLE: ZP714
TITLE: Activity of protegrins against yeast-phase Candida albicans
AUTHOR: Cho Y; Turner J S; Dinh N N; Lehrer R I (Reprint)
CORPORATE SOURCE: UNIV CALIF LOS ANGELES, SCH MED, DEPT MED, BOX 951690, 10833 LECONTE AVE, LOS ANGELES, CA 90095 (Reprint); UNIV CALIF LOS ANGELES, SCH MED, DEPT MED, LOS ANGELES, CA 90095; UNIV CALIF LOS ANGELES, SCH MED, INST MOL BIOL, LOS ANGELES, CA 90095
COUNTRY OF AUTHOR: USA
SOURCE: INFECTION AND IMMUNITY, (JUN 1998) Vol. 66, No. 6, pp. 2486-2493.
Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171.
ISSN: 0019-9567.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 39

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We used a two-stage radial diffusion assay to perform a structure-activity study of the antifungal effects of ***protegrin*** -1 (PG-1) on yeast-phase Candida albicans, While doing so, we computed MICs from the radial diffusion assay data by three methods and compared the respective values with results from colony count and broth microdilution assays. This allowed us to identify several technical ***modifications*** that improved the sensitivity and accuracy of radial diffusion assays. We found that both PG-1 and enantiomeric PG-1 (composed exclusively of D-amino acids) were potently fungicidal for yeast-phase C. albicans, The ***protegrins*** PG-2, -3, and -5, but not PG-4, were as effective as PG-1, At least one intramolecular ***disulfide*** bond was required to retain optimal candidacidal activity at physiological NaCl concentrations. Truncated variants of PG-1 that lacked its first four residues showed decreased candidacidal activity, although their activity against bacteria,vas substantially intact. Altering the beta-turn region (residues 9 to 12) of PG-1 or its variants further decreased candidacidal activity. These studies suggest that only 12 residues are needed to endow ***protegrin*** molecules with strong antibacterial activity and that at least 4 additional residues are needed to add potent antifungal properties. Thus, the 16-residue ***protegrin*** PG-2 likely represents the minimal structure needed for broad-spectrum antimicrobial

activity encompassing bacteria and fungi.

L7 ANSWER 16 OF 16 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 1998:326489 SCISEARCH
THE GENUINE ARTICLE: ZJ544
TITLE: Downsizing of an HIV-cell fusion inhibitor, T22 ([Tyr(5,12), Lys(7)]-polyphemusin II), with the maintenance of anti-HIV activity and solution structure
AUTHOR: Tamamura H (Reprint); Waki M; Imai M; Otaka A; Ibuka T; Waki K; Miyamoto K; Matsumoto A; Murakami T; Nakashima H; Yamamoto N; Fujii N
CORPORATE SOURCE: KYOTO UNIV, GRAD SCH PHARMACEUT SCI, SAKYO KU, KYOTO 60601, JAPAN (Reprint); SEIKAGAKU CORP, TOKYO RES INST, TOKYO 207, JAPAN; TOKYO MED & DENT UNIV, SCH MED, BUNKYO KU, TOKYO 113, JAPAN; KAGOSHIMA UNIV, SCH DENT, DEPT MICROBIOL & IMMUNOL, KAGOSHIMA 890, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: BIOORGANIC & MEDICINAL CHEMISTRY, (APR 1998) Vol. 6, No. 4, pp. 473-479.
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD, ENGLAND OX5 1GB.
ISSN: 0968-0896.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 27

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB T22 ([Tyr(5,12), Lys(7)]- ***polyphemusin*** II) has been shown to have strong anti-human immunodeficiency virus (HIV) activity comparable to that of 3'-azido-2',3'-dideoxythymidine (AZT). T22, an 18-residue peptide amide, takes an antiparallel beta-sheet structure that is maintained by two ***disulfide*** bridges. Herein we synthesized several shortened analogs of T22 in order to search for a more suitable lead compound. A 14-residue analog having one ***disulfide*** bridge, TW70 (des-[Cys(8,13), Tyr(9,12)]-[D-Lys(10), Pro(11)]-T22), was found to have highly potent activity comparable to that of T22, and to take an antiparallel beta-sheet structure similar to that of T22. This indicates that the molecular size of T22 can be reduced without loss of activity or significant change in the secondary structure, and that TW70 may represent a novel lead compound. Furthermore, ***modifying*** the N-terminal alpha-amino group of TW70 with a fluoresceinthiocarboooyl group, and the epsilon-amino group of D-Lys(8) at the turn portion with a 5-aminopentanoyl group remarkably increased the selectivity index (50% cytotoxic concentration/50% effective concentration).

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FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 17:15:26 ON 20 SEP 2002

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L1          3889 S ANTIBIOTIC PEPTIDE
L2          1065 S DEFINSIN OR PROTEGRIN OR TACHYPLESIN OR POLYPHEMUSIN
L3         40880 S (BETA SHEET) OR (BETA STRAND)
L4            20 S L1 (P) L3
L5           266 S (L2 OR L4 ) (P) (DISULFIDE OR CYSTEINE)
L6            79 DUPLICATE REMOVE L5 (187 DUPLICATES REMOVED)
L7            16 S L5 (P) MODIF?
L8         34260 S (ACTIVE SUBSTANCE)
L9         52477 S (THERAPEUTIC AGENT) OR (DIAGNOSTIC AGENT)
L10            0 S (L8 OR L9) (P) L5 (P) (CONJUGATE OR COVALENT)
L11            1 S L5 (P) (VECTOR? OR TRANSPORT?)
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